Polycomb-like 2 associates with PRC2 and regulates transcriptional networks during mouse embryonic stem cell self-renewal and differentiation.

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Public Summary:
We used embryonic stem cells to biochemically purify PRC2, a complex of proteins that regulates stem cell pluripotency. Analysis of this complex discovered a new regulator of pluripotency called Pcl2.

Scientific Abstract:
Polycomb group (PcG) proteins are conserved epigenetic transcriptional repressors that control numerous developmental gene expression programs and have recently been implicated in modulating embryonic stem cell (ESC) fate. We identified the PcG protein PCL2 (polycomb-like 2) in a genome-wide screen for regulators of self-renewal and pluripotency and predicted that it would play an important role in mouse ESC-fate determination. Using multiple biochemical strategies, we provide evidence that PCL2 is a Polycomb Repressive Complex 2 (PRC2)-associated protein in mouse ESCs. Knockdown of Pcl2 in ESCs resulted in heightened self-renewal characteristics, defects in differentiation, and altered patterns of histone methylation. Integration of global gene expression and promoter occupancy analyses allowed us to identify PCL2 and PRC2 transcriptional targets and draft regulatory networks. We describe the role of PCL2 in both modulating transcription of ESC self-renewal genes in undifferentiated ESCs as well as developmental regulators during early commitment and differentiation.